placebo-controlled trial designed to analyze the effect of amiodarone on mortality in heart failure patients.

Methods: Of the 274 deaths in the trial, 139 were categorized as SCD by the mortality committee. The precise time of SCD was available in 96 patients. Of these, 54 deaths occurred in the placebo group and 42 in the amiodarone group. The incidence of SCD was calculated for the following four time intervals: midnight–6 AM, 6 AM–noon, noon–6 PM, and 6 PM–midnight.

Results: There was a significant circadian variation with a morning peak between 6 AM and noon for all SCDs with known onset (relative distribution of SCD during the four time intervals: 14/42/18/27%, $p < 0.05$). The relative distribution of SCD was not different ($p = 0.2$) between the placebo group (7/44/22/26%) and the amiodarone group (21/38/12/29%).

Conclusion: SCD in CHF-STAT occurred predominantly between 6 AM and noon. Chronic amiodarone treatment did not affect this circadian pattern.

914-132 Electrophysiologic and Antifibrillatory Effects of Amiodarone and Desethylamiodarone

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The acute effects following intravenous amiodarone (A) are known to differ from its chronic effects, which may be influenced by its active metabolite desethylamiodarone (D). Accordingly, we investigated the effects of A (10 mg/kg, n = 7), D (10 mg/kg, n = 6), equal volume of vehicle (V, n = 7), and both A + D (B, same dose, n = 4) on the electrophysiologic effects and ventricular fibrillation threshold (VFT) in anesthetized pigs. VFT was defined as minimal current inducing fibrillation through a pacing catheter at the right ventricle using a "train" of electrical stimuli. The change from baseline value to post drug for VFT (ΔVFT), effective refractory period (ΔERP), ventricular fibrillation cycle length (ΔVFCL), QTc (ΔQTc), and drug concentration (C) are shown below:

	ΔVFT (mA)	ΔERP (ms)	ΔVFCL (ms)	ΔQTc (ms)	C (μg/ml)
D	9.5 ± 9.0	32 ± 29	28 ± 13*	40 ± 50	0.7 ± 0.5
A	8.0 ± 5.1*	26 ± 21	27 ± 9*	30 ± 20	1.1 ± 0.7
V	1.3 ± 3.2	5 ± 13	9 ± 16	3 ± 30	0 ± 0
B	36 ± 27*	75 ± 48			

*$p < 0.05$ vs vehicle

Conclusion: At similar concentration, desethylamiodarone and amiodarone produced similar electrophysiologic and antifibrillatory effects. While some of the effects are not significant from each drug alone, their combination appears to be additive or synergistic. These results explain the highly significant effects from chronic compared to acute amiodarone administration.

914-133 Torsades De Pointes Associated with Intravenous Haloperidol in Critically Ill Patients: Incidence and Influence on Length of Hospital Stay

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Background: Intravenous haloperidol (IVH) is commonly used for controlling agitation in critically ill patients. We observed 8 patients who developed torsades de pointes (TdP) in association with IVH therapy over a period of one year.

Patients and Methods: In this case-control study, 8 of 223 consecutive patients treated with IVH who developed TdP without any other metabolic, pharmacologic or neurologic risk factors known to cause TdP were compared with 41 patients who did not develop TdP selected randomly from the above group. Demographic data were collected, and QTc measurements were done in a blinded manner.

Results: The overall incidence of TdP associated with IVH in critically ill patients was 3.6%. The incidence of TdP in patients who received IVH ≥35 mg over 24 hours was 11.1% (7/63). Patients with or without TdP were demographically similar, including ventilator status. The odds ratios for TdP development were 33 and 14 in patients with QTc interval > 550 ms and for those who received IVH ≥35 mg over 24 hours, respectively. The length of hospital stay in patients with TdP was prolonged compared to the control group (19 ± 10 vs 12 ± 8 days, respectively, $p = 0.01$).

Conclusions: The incidence of TdP due to IVH in critically ill patients is substantial. The odds of development of TdP associated with IVH are higher in patients receiving ≥35 mg over 24 hours or with QTc interval of > 550 ms. IVH induced TdP in critically ill patients may be associated with prolonged hospital stay.

914-134 Influence of Autonomic Blockade on QT Dispersion in Man

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Autonomic nervous system modulates electrophysiologic properties of the ventricular myocardium, but little is known about the effects of autonomic activity on QT dispersion, which reflects the regional inhomogeneity of ventricular repolarization. The objective of this study is to evaluate the influence of pharmacological autonomic blockade on QT dispersion in healthy men. *Methods:* Propranolol (P: 0.2 mg/kg) or atropine (A: 0.04 mg/kg) were administered intravenously first to 21 healthy volunteers (HV, 32 yo), then second drug was given 6 minutes after the last dose of the first drug. Eleven HV received propranolol first (HVp), and another 10 atropine first (HVa). In each subject, QT intervals were measured from all 12 leads before and after each drug administration, and were corrected using Bazett's formula (QTc). Mean QTc interval of all 12 lead was calculated, and QTc dispersion (QTcd) was defined as the difference between maximal and minimal QTc interval. *Results:*

Group HVp	Baseline	P	P + A
MeanRR (msec)	929 ± 102	1,024 ± 112*	628 ± 23*
MeanQTc (msec)	369 ± 26	357 ± 12*	374 ± 11
QTcd (msec)	43.2 ± 7.0	23.5 ± 8.2*	44.8 ± 4.9

Group HVa	Baseline	A	A + P
MeanRR (msec)	964 ± 93.2	580 ± 14*	637 ± 32*
MeanQTc (msec)	365 ± 13	398 ± 14	388 ± 16
QTcd (msec)	39.2 ± 10.5	48.0 ± 10.7	38.6 ± 9.1

*$p < 0.05$, vs. each baseline value.

Conclusions: In healthy man, 1) adrenergic blockade shortened the QTc interval and decreased QT dispersion, on the other hand, atropine tended to increase QT dispersion. 2) QT dispersion also existed during complete autonomic blockade.

915 Computer Applications: Imaging, Neural Networks, and the Internet

Sunday, March 16, 1997, 5:00 p.m.–7:00 p.m.
Anaheim Convention Center, Hall E
Presentation Hour: 5:00 p.m.–7:00 p.m.

915-110 Implementation of an Internet/World-Wide-Web Original Database for Supporting Multicenter Clinical Trials

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Internet and the World-Wide-Web (WWW) have not yet been used for collecting clinical and treatment data from cardiac patients. To exploit the unique potential of the integration of internet-type connections, World-Wide-Web and remote SQL-database access, we developed an original application for supporting a multicenter clinical study for the prognostic stratification of patients with unstable angina. This study is aimed at assessing which clinical variables best predict outcome in homogeneous classes of unstable angina patients. It involves 50 coronary care units evenly distributed throughout the country and structured in a stratified system of care including community hospitals, secondary and tertiary referral centers. The study database has been developed to fulfill the data requirements of the protocol. Collectable data span from past medical history to treatment, diagnostic examinations and follow-up; they are structured in 16 relational tables. The Oracle-web engine provides the SQL database back-end while the front-end has been developed in standard HTML with Netscape 3.x extensions enabled. Data validation is assured by back-end SQL rules and by front-end JAVA applets. Referential integrity is maintained by the engine, and access security is granted by the combined Netscape/Oracle properties, the WWW-server and the SQL-server being two separate UNIX-based computers. The database has been successfully tested with run-in test-data, while the multicenter trial is currently in the initial patient enrollment phase.

Our approach fosters clinical studies in a new era where available telematic technologies allow easier and faster collection and validation of patients' data, on-line monitoring of the ongoing activities and wider dissemination of intermediate and final results.